UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

14/APR/2010

MEMORANDUM

Subject:	Name of Pesticide Product:	NEUDORFF ANT BUFFET
	EPA File Symbol:	67702-GN
	DP Barcode:	D372863
	Decision No.:	425258
	Action Code:	R310
	PC Code:	110003 Spinosad

From: Rick J. Whiting, Biologist
Technical Review Branch (TRB)
Registration Division (7505P)

To: Samantha Hulkower / Mark Suarez, RM Team 13
Insecticide Branch
Registration Division (7505P)

Applicant: W. Neudorff GMbH KG
An de Mühle 3
31860 Emmerthal, Germany

FORMULATION FROM LABEL:

Active Ingredient(s):		% by wt
110003	Spinosad [a mixture of Spinosyn A (CAS No. 131929-60-7) & Spinosyn D (CAS No. 131929-63-0)]	0.015
Inert Ingredient(s):		99.985
	Total:	100.000%

ACTION REQUESTED: The Risk Manager requests: "Please review the following acute toxicity data for a new product from a registered active ingredient."

BACKGROUND: W. Neudorff GMbH KG has submitted five acute toxicity studies, Basic and Alternate Formulation CSFs dated December 9, 2009 and a proposed label to support the registration of NEUDORFF ANT BUFFET, EPA File Symbol 67702-GN. The registrant is also requesting a waiver for the acute inhalation study. The acute oral and dermal studies were conducted at Stillmeadow, Inc. and assigned MRID numbers 47940203 and 47940204. The primary eye and dermal irritation studies and the dermal sensitization study were conducted at Laboratory of Pharmacology & Toxicology GmbH & Co. KG and assigned MRID numbers 47940206, 47940205 and 47940207.

COMMENTS AND RECOMMENDATIONS:

1. The five studies have been reviewed and are classified as Acceptable.

2. In a letter to EPA dated December 9, 2009 (MRID 47940200) the registrant stated "A study was not submitted for the Acute Inhalation Toxicity data requirement, due to the fact that per 40CFS 158.500(e)(4) a study is not applicable as the product does not consist of a respirable material under the conditions of use."

TRB did not consider the above information to be adequate to approve the data waiver and requested the risk manager, Samantha Hulkower, to contact the registrant and request a more detailed rationale for the data waiver request. The following information is from a letter dated April 12, 2010 emailed to EPA by the registrant:

> 1) Physical composition: Neudorff Ant Buffet consists of a bait solution that is either enclosed in sealed bait stations (non-refillable) or poured in small quantities into bait stations (refillable), from where it is taken by worker ants back to an ant colony. Once sealed in the bait station or poured into the bait station the water evaporates out and the solution hardens.
>
> 2) Method of application: In all cases the bait solution is either already sealed in the bait stations or is poured in small amounts into refillable bait stations. The bait solution is never sprayed or applied in a manner that will result in a gas, vapor, aerosol or particulate. Neither the physical state nor the method of application would create a respirable material.
>
> In addition, the inhalation toxicity of the active ingredient is low, with a reported LC5O greater than 5.18 mg/L (Yano et al, 2002). The inert ingredients in Neudorff Ant Buffet are all low in toxicity and some are present in very small quantities such that their contribution to any potential inhalation toxicity would be minimal. It is also worth mentioning that, based on the acute toxicity data submitted, the end-use formulation is Toxicity Category IV for all other routes of exposure (oral, dermal, eye). There would be no reason to expect the formulation would have any toxicity or adverse effects via the inhalation route of exposure.

Based on the additional information provided by the registrant, TRB agrees that an acute inhalation study in not required and agrees to waive the study. For the acute toxicity profile, the acute inhalation study will be assigned a Toxicity Category of IV.

3. The acute toxicity profile for NEUDORFF ANT BUFFET, EPA File Symbol 67702-GN, is as follows:

Acute oral toxicity	IV	Acceptable	MRID 47940203
Acute dermal toxicity	IV	Acceptable	MRID 47940204
Acute inhalation toxicity	IV	Waived	
Primary eye irritation	IV	Acceptable	MRID 47940206
Primary skin irritation	IV	Acceptable	MRID 47940205
Dermal sensitization	Negative	Acceptable	MRID 47940207

4. Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System:

PRODUCT ID #: 067702-00030

PRODUCT NAME: NEUDORFF ANT BUFFET

PRECAUTIONARY STATEMENTS

SIGNAL WORD: CAUTION [Optional]

Hazards to Humans and Domestic Animals:

Wear: Long-sleeved shirt and long pants, socks, shoes, and gloves.

First Aid: [Not required. Registrant can use Category III statements.]

5. The Basic and Alternate Formulation CSFs dated December 9, 2009 for the proposed product should also be reviewed and accepted by the TRB Product Chemistry Team.

Reviewer: Rick J. Whiting **Date: April 14, 2010**
Risk Manager (EPA): 13

STUDY TYPE: Acute Oral Toxicity - Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid)

CITATION: Kuhn, J. (2008) NEU 1262 I: Acute Oral Toxicity Study: Up & Down Procedure (UDP) in Rats: Final Report. Project Number: 12324-08. Unpublished study prepared by Stillmeadow, Inc. 12 p. November 19, 2008. MRID 47940203

SPONSOR: Eco-Care Technologies, Inc., 8233 Thomson Place, Saanichton BC Canada V8M 1S1

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 47940203), three young adult female Sprague-Dawley rats (age: 9 weeks; weight: 171-181 g; source: Texas Animal Specialties, Humble, TX) were given a single oral dose of undiluted NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid). An individual dose was calculated for each animal based on its fasted body weight and administered by gavage at a volume of 4.57 ml/kg. Following the Up and Down Procedure, an initial limit dose of 5000 mg/kg of the test material was administered to one female rat by oral gavage. Due to the absence of mortality in this animal, two additional animals received the same dose level. Observations for mortality and clinical/behavioral signs of toxicity were made at least three times on the day of dosing (Day 0) and at least once daily thereafter for 14 days. Individual body weights were recorded just prior to dosing and on Days 7 and 14, or at the time of discovery after death. All animals were subjected to gross necropsy.

All animals survived, gained body weight, and appeared active and healthy during the study. There were no signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior. No gross abnormalities were noted for any of the animals necropsied at the conclusion of the 14-day observation period.

Oral LD_{50} Females > 5000 mg/kg bw

Based on the Oral LD_{50} in females, NEU 1262 I is classified as EPA Toxicity Category IV.

This acute oral study is classified as Acceptable. It does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Individual animals were dosed as follows:

Limit Test

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short-Term Outcome	Long-Term Outcome
1	291	5000	S	S
2	292	5000	S	S
3	293	5000	S	S

S = survival D = death

Statistics: Acute Oral Toxicity (Guideline 425) Statistical Program (Westat, version 1.0, May 2001) was used for all data analyses including: dose progression selections, stopping criteria determinations and/or LD_{50} and confidence limit calculations.

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Test/Substance: NEUDORFF ANT BUFFET
Test type: Limit Test
Limit dose (mg/kg): 5000
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	291	5000	O	O
2	292	5000	O	O
3	293	5000	O	O

(X = Died, O = Survived)

Dose Recommendation: The limit test is complete.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
5000	3	0	3
All Doses	3	0	3

Statistical Estimates: The LD50 is greater than 5000 mg/kg.

A. Mortality: There was no mortality.

B. Clinical observations: There were no signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior.

C. Gross Necropsy: No gross abnormalities were noted for any of the animals necropsied at the conclusion of the 14-day observation period.

D. Reviewer's Conclusions: TRB agrees with the study author's conclusions. Based on the LD_{50} in females, NEU 1262 I is classified as EPA Toxicity Category IV.

E. Deficiencies: None.

Reviewer: Rick J. Whiting **Date: April 14, 2010**
Risk Manager (EPA): 13

STUDY TYPE: Acute Dermal Toxicity - Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid)

CITATION: Kuhn, J. (2008) NEU 1262 I: Acute Dermal Toxicity Study in Rats: Final Report. Project Number: 12325-08. Unpublished study prepared by Stillmeadow, Inc. 12 p. November 19, 2008. MRID 47940204

SPONSOR: Eco-Care Technologies, Inc., 8233 Thomson Place, Saanichton BC Canada V8M 1S1

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 47940204), groups of five young Sprague-Dawley rats/sex (age: 11 weeks; weight: 307-338 g for males and 201-224 g for females; source: Texas Animal Specialties, Humble, TX) were exposed to a single dermal application of 5050 mg/kg (4.62 ml/kg) body weight of undiluted NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid) for 24 hours. On the day prior to treatment, each animal was prepared by clipping the dorsal surface of the trunk free of hair to expose approximately 10% of the total body surface area. All animals were treated with the undiluted test material. An individual dose was calculated for each animal based on its Day 0 body weight just before exposure. The test material was applied evenly to each exposure area in a thin, uniform layer. The area of application was covered with a 2 x 4 inch surgical gauze patch and secured with non-irritating tape. The trunk of each animal was then wrapped with vet wrap that was secured in place with non-irritating adhesive tape to prevent possible ingest of the test material. After the exposure period, the wrappings were removed and the test sites were gently washed with room temperature tap water and a clean cloth to remove as much residual test material as possible.

Observations for mortality and clinical/behavioral signs of toxicity were made at least three times on the day of dosing (Day 0) and at least once daily thereafter for 14 days. Individual body weights were recorded prior to dosing and on Days 7 and 14. Observations for evidence of dermal irritation were made at approximately 60 minutes after removal of wrappings and on Days 4, 7, 11 and 14. All study animals were subjected to gross necropsy and all abnormalities were recorded.

All animals survived, gained body weight, and appeared active and healthy during the study. There were no signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior. No gross abnormalities were noted for any of the animals necropsied at the conclusion of the 14-day observation period.

Dermal LD_{50} Males > 5050 mg/kg bw
Dermal LD_{50} Females > 5050 mg/kg bw
Dermal LD_{50} Combined > 5050 mg/kg bw

Based on the LD_{50}, NEU 1262 I is classified as EPA Toxicity Category IV.

This acute dermal study is classified Acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
5050	0/5	0/5	0/10

A. Mortality: There were no deaths.

B. Clinical observations: There were no signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior.

C. Gross Necropsy: No gross abnormalities were noted for any of the animals necropsied at the conclusion of the 14-day observation period.

D. Reviewer's Conclusions: TRB agrees with the study author's conclusions. Based on the LD_{50}, NEU 1262 I is classified as EPA Toxicity Category IV.

E. Deficiencies: None.

Reviewer: Rick J. Whiting **Date: April 14, 2010**
Risk Manager (EPA): 13

STUDY TYPE: Primary Eye Irritation - Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL: NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid)

CITATION: Leuschner, P. (2007) Acute Eye Irritation/Corrosion of NEU 1262I in Rabbits. Project Number: 21764. Unpublished study prepared by Laboratory of Pharmacology & Toxicology GmbH & Co. KG. 28 p. . August 1, 2007. MRID 47940206

SPONSOR: W. Neudorff GmbH KG, An der Mühle 3, 31860 Emmerthal, Germany

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 47940206), 0.1 mL of NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid) was instilled into the conjunctival sac of the right eye of three young adult male Himalayan rabbits (age: 4-5 months; weight: 2.0-2.3 kg; source: LPT Laboratory of Pharmacology and Toxicology GmbH & Co. KG, branch Löhndorf, 24601 Löhndorf/Post Wankendorf, Germany). The other untreated eye served as a control. Twenty-fours hours after instillation, the treated eye was rinsed with 20 mL of a NaCl solution. Ocular irritation was evaluated using a silt lamp at 1, 24, 48 and 72 hours.

No corneal opacity or iritis was observed in any rabbit during the study. Conjunctival redness (score 1) was observed in 3/3 eyes at 1 hour. All ocular irritation was resolved by 24 hours.

In this study, the formulation was non-irritating. NEU 1262 I is classified as EPA Toxicity Category IV for primary eye irritation.

This study is classified as Acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

	Number "positive"/number tested			
	Hours			
Observations	**1**	**24**	**48**	**72**
Corneal Opacity	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3
Conjunctivae:				
Redness*	0/3	0/3	0/3	0/3
Chemosis*	0/3	0/3	0/3	0/3

*Score of 2 or more required to be considered "positive."

A. Observations: No corneal opacity or iritis was observed in any rabbit during the study. Conjunctival redness (score 1) was observed in 3/3 eyes at 1 hour. All ocular irritation was resolved by 24 hours.

B. Results: NEU 1262 I was considered non-irritating due to the lack of any "positive" scores.

C. Reviewer's Conclusions: TRB agrees with the study author's conclusions. NEU 1262 I is classified as EPA Toxicity Category IV.

D. Deficiencies: None.

Reviewer: Rick J. Whiting **Date: April 14, 2010**
Risk Manager (EPA): 13

STUDY TYPE: Primary Dermal Irritation - Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid)

CITATION: Leuschner, P. (2007) Acute Dermal Irritation/Corrosion Test (Patch Test) of NEU 1262I in Rabbits. Project Number: 21763. Unpublished study prepared by Laboratory of Pharmacology & Toxicology GmbH & Co. KG. 27 p. August 1, 2007. MRID 47940205

SPONSOR: W. Neudorff GmbH KG, An der Mühle 3, 31860 Emmerthal, Germany

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 47940205), three male young adult Himalayan rabbits (age: 4-5 months; weight: 2.1-2.3 kg; source: LPT Laboratory of Pharmacology and Toxicology GmbH & Co. KG, branch Löhndorf, 24601 Löhndorf/Post Wankendorf, Germany) were dermally exposed to NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid). Approximately 24 hours before the test, the fur was removed by shaving the dorsal area of the trunk of the animals. A dose of 0.5 mL of the test material was applied to the test site area (approximately 6 cm^2) and the test was covered with a gauze patch. The patch was held in place with non-irritating tape for the duration of the 4 hour exposure period. The surrounding untreated skin served as a control. After the exposure period the patch was removed and the skin sites were evaluated for dermal irritation at 1, 24, 48 and 72 hours.

No dermal irritation was observed in any animal throughout the duration of the study. Primary Dermal Irritation Index (PDII) = 0.0.

In this study, the formulation was non-irritating. NEU 1262 I is classified as EPA Toxicity Category IV for primary dermal irritation.

This study is classified as Acceptable. It does satisfy the guideline requirement for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

INDIVIDUAL SKIN IRRITATION SCORES

ERYTHEMA/EDEMA

Animal No.	Sex	Hours After Patch Removal			
		1	24	48	72
1	M	0/0	0/0	0/0	0/0
2	M	0/0	0/0	0/0	0/0
3	M	0/0	0/0	0/0	0/0

A. Observations: No dermal irritation was observed in any animal throughout the duration of the study.

B. Results: Primary Dermal Irritation Index (PDII) = 0.0

C. Reviewer's Conclusions: TRB agrees with the study author's conclusions. NEU 1262 I is classified as EPA Toxicity Category IV.

D. Deficiencies: None.

Reviewer: Rick J. Whiting **Date: April 14, 2010**
Risk Manager (EPA): 13

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406, 429

TEST MATERIAL: NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid)

CITATION: Leuschner, P. (2007) Examination of NEU 1262 I in the Skin Sensitization Test in Guinea Pigs According to Magnusson and Kligman (Maximization Test). Project Number: 21765. Unpublished study prepared by Laboratory of Pharmacology & Toxicology GmbH & Co. KG. 39 p. September 5, 2007. MRID No. 47940207

SPONSOR: W. Neudorff GmbH KG, An der Mühle 3, 31860 Emmerthal, Germany

EXECUTIVE SUMMARY: A dermal sensitization study (Magnusson and Kligman; MRID 47940207) was conducted with young adult male Dunkin-Hartley guinea pigs (age: 30 days; weight: 264-355 g; source: Charles River Deutschland GmbH, Stolzenseeweg 32-36, 88353 Kißlegg, Germany) to determine the potential for NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid) to produce sensitization after repeated topical applications.

Procedure for Preliminary study (from pages 13-14 of the study):

For the preliminary test, eight animals were used: 6 animals for the topical administration and 2 animals for the intracutaneous administration. The allocation of different test sites of the animals was alternated in order to minimize site-to-site variations in response. The shoulder and the flank region of the animals were shaved or shaved and depilated (approximately 5 x 5 cm).

(a) Intracutaneous: 0.1 ml of the prepared test item was administered intracutaneously (shoulder region). Three concentrations of the test item were injected intradermally into one, 3 further concentrations into a second animal.

(b) Topical: The test area of 3 animals each was shaved or depilated. 2 mL of the test preparation was spread over a filter paper (2 x 4 cm) and applied to the test area and held in contact by an occlusive dressing. Two concentrations each were applied to the shaved or shaved and depilated flanks of 3 animals each. The occlusive dressing and the filter paper containing the test item were removed after 24 or 46 hours end the application sites were assessed immediately, 24 and 48 (depilated) or immediately and 24 hours (non-depilated) after remove) of the filter paper for erythema and oedema.

Results from the Preliminary study (from page 20 of the study):

Six concentrations of NEU 1262 I were tested by intracutaneous injection: 0.01, 0.1, 0.5, 1, 5 and 10% suspensions in *aqua ad injectabilia*. No skin reactions were observed up to the top concentration of 10%. Six concentrations of NW 1262 I were tested by topical application: 1, 5, 10, 25 and 50% suspensions in *aqua ad injectabilia* and the undiluted test item.

Undepilated and depilated skin: No skin reactions were observed neither with the dilutions nor with the undiluted test item. Hence, it was decided to use a 10% concentration for the 1st (Intracutaneous) induction stage, the undiluted test item for the 2nd (topical) induction stage and for the challenge.

Procedure for the Main Study (from pages 15-17 of the study):

The test item was diluted in *aqua ad injectabilia*. Fifteen animals were randomly allocated to 2 groups: Group 1 (vehicle control) and Group 2 (NEU 1262 I). The following concentrations were employed for Test Group 2 animals: Stage 1: intracutaneous 10% concentration of NEU 12621 in *aqua ad injectabilia*; Stage 2: the undiluted test item and Stage 3: undiluted test item.

Stage 1 (Induction) - Day 0: Three pairs of intradermal injections were given in the shoulder region which was cleared of hair so that one of each pair lay on each side of midline.

(1) 0.1 mL Freund's complete adjuvant7 (FCA) (diluted 1: 1 (v/v) with physiological saline)
(2) 0.1 ml of the test Item (concentration see above)
(3) 0.1 mL of the test item In a 1 + 1 mixture (v/v) FCA/physiological saline

In injection 3, the final concentration of the test item was equal to that in injection 2.

Injections (1) and (2) were given close to each other and nearest the head, while (3) was given towards the caudal part of the test area.

Day 8: As the test item was not irritating to the undepilated skin of the test animals in the preliminary study, the fur was shaved from the application area and the exposed skin was coated with 0.5 mL sodium lauryl sulfate 10% in vaseline in order to induce a local irritation.

Stage 2 (Induction) – Day 7: Seven days after the intracutaneous injection, the shoulder region of the same animals was shaved again and treated topically using the patch-teat technique (exposure time: 48 hours).

Stage 3 (Challenge) - Day 21: Two weeks after the topical application (corresponds to a monitoring period of 21 days) the flanks of the same animals were shaved and depilated for a further topical application using the patch-test technique. The filter paper containing the test item was applied to the left flank, the filter paper with the vehicle to the right flank of the animal (exposure time: 24 hours). Twenty-one hours after the filter paper had been removed, the treated skin was cleaned.

Vehicle control group 1: *aqua ad injectabilia* - The vehicle reference animals were treated in the same way as the animals of the test group (2), but received *aqua ad injectabilia* instead of the test item. However, in Stage 3 the left flank was treated with the test item, the right flank with the vehicle i.e. in the same way as the test group (2).

The dermal irritation results of the first induction exposure were evaluated at 24 and 48 hours and for the second induction at 48 and 72 hours. On Days 23 and 24, 21 hours after removing the filter paper the challenge area was cleaned and cleared of hair if necessary. Three hours later (at 48 hours from the start of challenge application) the dermal irritation was observed and

recorded. Twenty-four hours after this observation, a second observation (72 hours) was made and recorded.

Results for the Main Study (from page 20 of the study):

A 10% suspension of NEU 1262 I in *aqua ad injectabilia* chosen for the 1st (intracutaneous) induction stage did not reveal any skin reactions. 2 mL of the undiluted test item chosen for the 2nd (topical) induction stage was not irritating to the shaved skin in the preliminary experiment. Hence, in the main study the skin was coated with sodium lauryl sulfate on the day before stage 2 induction in order to induce a local irritation.

The challenge with 2 mL of the undiluted test item/animal revealed no skin irritation in any animal and, thus, the test Item had no sensitising properties.

The vehicle reference revealed no skin reactions per se, either.

Behaviour remained unchanged. The body weight gain of the animals treated with NEU 1262 I was within the range of the vehicle control during the experiment.

Based on the results of this study, NEU 1262 I is not considered to be a dermal sensitizer.

This study is classified as Acceptable. It does satisfy the guideline requirement for a dermal sensitization study (OPPTS 870.2600; OECD 406, 429) in the Guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. PROCEDURE:

A. Induction: The test item was diluted in *aqua ad injectabilia*. Fifteen animals were randomly allocated to 2 groups: Group 1 (vehicle control) and Group 2 (NEU 1262 I). The following concentrations were employed for Test Group 2 animals: Stage 1: intracutaneous 10% concentration of NEU 12621 in *aqua ad injectabilia*; Stage 2: the undiluted test item and Stage 3: undiluted test item.

Stage 1 (Induction) - Day 0: Three pairs of intradermal injections were given in the shoulder region which was cleared of hair so that one of each pair lay on each side of midline.

(1) 0.1 mL Freund's complete adjuvant7 (FCA) (diluted 1: 1 (v/v) with physiological saline)
(2) 0.1 ml of the test Item (concentration see above)
(3) 0.1 mL of the test item In a 1 + 1 mixture (v/v) FCA/physiological saline

In injection 3, the final concentration of the test item was equal to that in injection 2.

Injections (1) and (2) were given close to each other and nearest the head, while (3) was given towards the caudal part of the test area.

Day 8: As the test item was not irritating to the undepilated skin of the test animals in the preliminary study, the fur was shaved from the application area and the exposed skin was coated with 0.5 mL sodium lauryl sulfate 10% in vaseline in order to induce a local irritation.

Stage 2 (Induction) – Day 7: Seven days after the intracutaneous injection, the shoulder region of the same animals was shaved again and treated topically using the patch-teat technique (exposure time: 48 hours).

B. Challenge: Stage 3 (Challenge) - Day 21: Two weeks after the topical application (corresponds to a monitoring period of 21 days) the flanks of the same animals were shaved and depilated for a further topical application using the patch-test technique. The filter paper containing the test item was applied to the left flank, the filter paper with the vehicle to the right flank of the animal (exposure time: 24 hours). Twenty-one hours after the filter paper had been removed, the treated skin was cleaned.

C. Naive Controls: Vehicle control group 1: *aqua ad injectabilia* - The vehicle reference animals were treated in the same way as the animals of the test group (2), but received *aqua ad injectabilia* instead of the test item. However, in Stage 3 the left flank was treated with the test item, the right flank with the vehicle i.e. in the same way as the test group (2).

II. RESULTS and DISCUSSION:

A. Reactions and duration:

B. Positive control: Positive control data were obtained from the historical background of Laboratory of Pharmacology & Toxicology GmbH & Co. KG. The positive control group was not tested concurrently with the main study but is a historical background group from a study performed in May/June 2007.

Dunkin-Hartley guinea pigs treated with benzocaine in 40% ethanolic 0.9% NaCl solution exhibited a sensitising reaction in all animals in form of a discrete or patchy erythema (grade 1) or a moderate and confluent erythema (grade 2).

C. Reviewer's Conclusions: TRB agrees with the study author that NEU 1262 I is not a dermal sensitizer.

D. Deficiencies: None.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D372863
2. **PC CODE:** 110003
3. **CURRENT DATE:** 14/APR/2010
4. **TEST MATERIAL:** NEU 1262 I (Spinosad – 0.017%; Batch No. 080 607; Density: 1.0942 g/mL; light blue liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity / rat Stillmeadow, Inc. 12324-08 / November 19, 2008	47940203	LD_{50} > 5000 mg/kg (females)	IV	A
Acute dermal toxicity / rat Stillmeadow, Inc. 12325-08 / November 19, 2008	47940204	LD_{50} > 5050 mg/kg (males and females)	IV	A
Primary eye irritation / rabbit Laboratory of Pharmacology & Toxicology GmbH & Co. KG 21764 / August 1, 2007	47940206	Non-irritating	IV	A
Primary dermal irritation / rabbit Laboratory of Pharmacology & Toxicology GmbH & Co. KG 21763 / August 1, 2007	47940205	Non-irritating	IV	A
Dermal sensitization / guinea pig Laboratory of Pharmacology & Toxicology GmbH & Co. KG 21765 / September 5, 2007	47940207	Negative	---	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, W = Waived